Arch. Pharm. Chemi Sci. Ed. 5, 1977, 178-193. Received August 3, 1977

Control of fluidized bed granulation

II. Estimation of droplet size of atomized binder solutions

Torben Schæfer & Ole Wørts***

Water and aqueous solutions of gelatine, polyvinylpyrrolidone, sodium carboxymethylcellulose and methylcellulose in varying concentrations were atomized in a pneumatic nozzle ordinarily used for fluidized bed spray granulation. The droplet size distributions were estimated by taking photo-micrographs of the droplets collected on oil-covered slides and were described by a logistic equation.

The mean droplet size increased with decreasing air-to-liquid mass ratio and liquid flow rate and with increasing viscosity and spray angle. The diameter of the liquid orifice did not affect droplet size except under extreme experimental conditions. An empirical droplet size equation permitting an approximate prediction of the mass median diameter for the nozzle used in the experiments was derived.

Fluidized bed granulation is carried out by spraying an atomized binder solution on the fluidized starting materials. It has been shown by *Thurn* (25) that a decrease in droplet size resulted in decreased size of the final granules, but only a few experiments were carried out and no simple correlation was found.

Several authors have shown that increased nozzle air flow results in a decrease in granule size (4,9,19,21,23), whereas others found no effect of this factor (14,16). However, a direct comparison of the results of different authors is not possible, since droplet sizes have not been examined.

Davies & Gloor (5) concluded that type and concentration of binder profoundly affected glanule size. To account for these results it is necessary to examine the effect of these factors on droplet size of the atomized binder solution. In a previous paper (23) the influence of spray angle on granule size was considered to be a function of droplet size, an assumption which can, however, only be confirmed by a droplet size estimation.

---

* The Royal Danish School of Pharmacy, Department of Pharmaceutics, 2 Universitetsparken, DK-2100 Copenhagen, Denmark.

** Novo Industri A/S, Pharmaceutical Research and Development Laboratory, Novo Allé, DK-2880 Bagsværd, Denmark.

The reason that droplet size of binder solutions generally has not been investigated in the above-mentioned works may be that the methods of analysis usually are inaccurate and very time-consuming. *Bürkholz* (1) has reviewed such methods. An analysis can be performed by taking photographs of droplets directly in the spray cone (11,26) or after collection in a viscous oil (6,7,25), but various indirect methods may also be used (7,8,18,20). The main sources of error are collection of an unrepresentative sample as well as evaporation, coalescense and flattening of the droplets (7).

Usually the nozzles applied for fluidized bed granulation are pneumatic. *Thurn* (25) found a pneumatic nozzle to be more suitable for granulation in a fluidized bed than a pressure nozzle, an alteration of droplet size being difficult by use of the latter.

Empirical equations have been set up to estimate the mean droplet size obtained by pneumatic atomization (8,13,15), yet the equation of *Kim & Marshall* (13) seems to be more generally applicable. The mean droplet size is primarily influenced by nozzle construction, air-to-liquid mass ratio, and the dynamic force of atomizing air, and secondarily by surface tension, density, and viscosity of the liquid and density of the atomizing air (13).

The purpose of this work has been to select a simple method suitable for droplet size analysis under the experimental conditions used for fluidized bed granulation and to use the method to examine the applicability of the existing droplet size equations for the actual nozzle. If necessary an additional equation should be derived. Relationships between droplet size and granule size will be described in a later paper.

Experimental

Binder solutions

Water and aqueous solutions of gelatine (Ph.Nord. 63), polyvinylpyrrolidone (Kollidon® 25 and 90, BASF), sodium carboxymethylcellulose (7L1, Hercules) (CMC) and methylcellulose (15, DAK 63) (MC) in varying concentrations were used. As the viscosity of binder solutions may be affected by the method of preparation and storage conditions (2,3,12,22,24), the solutions were prepared under accurately specified experimental conditions as described below.

Kollidon 25, Kollidon 90 and CMC were dispersed by addition of water at room temperature and were left to stand for about 24 h with occasional stirring. Gelatine solutions were made immediately before use by dissolving gelatine powder in water at 50° C. MC was dispersed in half the required amount of water at 80° C. The mixture was stirred at intervals for 30 min and then filled up to the desired weight with ice water, after which the dispersion was left to stand for about 24 h with occasional stirring. The final binder solutions were kept at the desired temperature in a thermostat for about 1 h before use.

Table 1. Combinations of air flow rate (Nm^3/h) and liquid flow rate used in the experiments.

Liquid flow rate	Air-to-liquid mass ratio				
	0.86	1.15	1.43	2.01	2.58
100 g/min	4.00 Nm^3/h	5.34 Nm^3/h	6.67 Nm^3/h	9.33 Nm^3/h	12.0 Nm^3/h
150 g/min	6.00 Nm^3/h	8.00 Nm^3/h	10.0 Nm^3/h	14.0 Nm^3/h	18.0 Nm^3/h
200 g/min	8.00 Nm^3/h	10.7 Nm^3/h	13.3 Nm^3/h	18.7 Nm^3/h	–

Nozzle

A pneumatic nozzle (Schlick, model 941-943/7) generally used in a fluidized bed spray granulator (Glatt, model WSG 15) was used. Unless otherwise stated the air dome on the nozzle head was set in number 5 position (23), and the diameter of the liquid orifice was 1.8 mm. Air and liquid flow rates were controlled as previously described (24); the combinations used for the atomization experiments are shown in Table 1.

Methods

Viscosity. The viscosity of all solutions was measured with a falling ball viscometer (Haake, model B/BH). Further, a rotational viscometer (Brookfield, model LVT) was used for some of the solutions.

Surface tension. Surface tension was measured with a tensiometer (Krüss, model K8600E).

Droplet size analysis. A modification of the method described by *Golitzine* (7) was used. A slide covered with a viscous lubricating oil (Macoma R85, Shell) was manually passed across the spray cone at a distance of about 45 cm below the nozzle orifice. A photo-micrograph of the droplet sample was then taken immediately. The negative was enlarged to a total magnification of 50 times (Fig. 1).

To delay evaporation of droplets after sampling the analysis was performed in a room with a relative humidity of at least 80 %. To reduce the uncertainty from

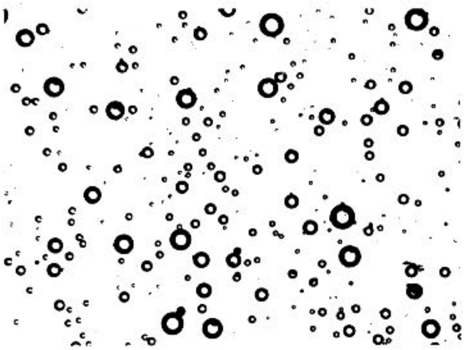

Figure 1. Example of a photograph of a droplet sample. Magnification: 50 times (excl. a photographic reduction of 50 %). d_{50} = 111 µm. Binder solution: Gelatine 4 %, 40°. Liquid flow rate: 150 g/min. Air flow rate: 8 Nm^3/h.

the sampling procedure 10 photographs were sampled for a single droplet size analysis, and the mass median diameter, d_{50}, was estimated by counting a total of about 1000 droplets. The droplet size distribution was characterized as described later.

Results and discussion

Evaluation of the method for droplet size analysis

To examine the influence of evaporation of droplets photographs were taken at varying intervals after sampling (Table 2). As increased viscosity of the atomized liquid may delay evaporation, water was selected for the experiments. Normally a photograph is taken within 15 sec after collection of the sample, and thus the results obtained show that evaporation has no remarkable influence on the estimated droplet size of aqueous solutions.

In over-exposure of the sample droplets coalesce, which results in a systematic error. The influence of droplet concentration on the estimated droplet size is shown in Table 3. The concentration was varied by changing the velocity of the slide. It can be seen from the Table that droplet concentrations lower than 50 droplets per mm^2 had no appreciable influence, whereas a remarkable increase in droplet size, due to coalescense, was observed at higher values. In the subsequent experiments concentrations below this limit were used.

The method is not applicable at liquid flow rates exceeding ab. 200 g/min, since the maximum velocity of the manually handled slide sets a lower limit to droplet concentration.

It has not been possible to examine the flattening of droplets after collection in oil. The viscosity of the oil makes it probable that they retain their spherical shape unless droplet sizes are extremely high when flattening may cause a systematic error.

Table 2. Influence of evaporation on estimated droplet size after collection of a droplet sample.
Liquid: Water, 30° C. Liquid flow rate: 200 g/min.
Air flow rate: 12 Nm^3/h.

Number of droplets counted	Time after collection	Droplet size d_{50}, µm
1078	10 sec	83
1075	½ min	80
1125	1 min	80
1077	2 min	83

Table 3. Influence of droplet concentration on estimated droplet size.
Liquid: Water, 30° C. Liquid flow rate: 200 g/min.
Air flow rate: 12 Nm³/h.

Number of droplets counted	Droplet concentration Number of droplets > 15 μm per mm²	Droplet size d_{50}, μm
1078	ca. 30	83
1479	ca. 40	78
1237	ca. 50	90
1691	ca. 75	119

The relative standard deviation of the droplet size estimation was found to be about 7 % at mass median diameters below ca. 150 μm. At higher values an increase in the relative standard deviation was observed, probably due to flattening and difficulties in collecting a representative sample.

Viscosity of binder solutions

The viscosity of the solutions was measured by the falling ball viscometer in the temperature range 20-80° C with the exception of solutions of gelatine and MC where gelation occurred when below ca. 40° C (gelatine)

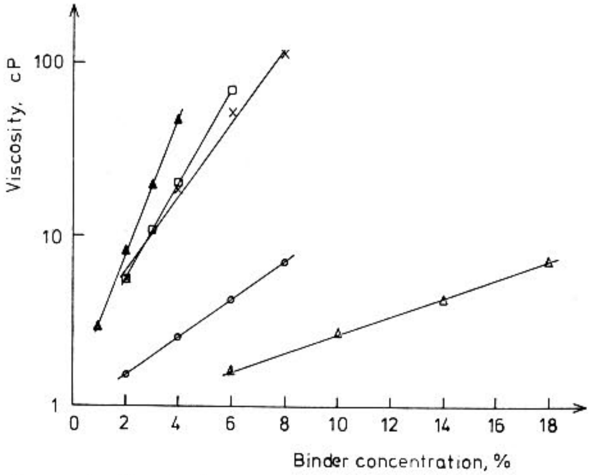

Figure 2. Correlation between binder concentration and viscosity of the binder solution.
Liquid temperature: 40° C (MC: 30° C).

○: gelatine △: Kollidon 25 x: Kollidon 90
□: CMC ▲: MC

and above ca. 30° C (MC). Fig. 2 shows the results derived at the temperatures ordinarily used in the experiments.

Since atomization with the peristaltic pump and the nozzle system used was impossible at viscosities exceeding ab. 150 cP, a low viscosity type of CMC was applied. It is a prior requirement to the use of a falling ball viscometer that the binder solutions are ideal viscous liquids, and therefore solutions of the two highest concentrations (see Fig. 2) of every binder were investigated with the Brookfield viscometer. CMC 6 % and Kollidon 90 8 % showed a slight tendency to exhibit pseudoplastic behaviour, while no remarkable deviations from the ideal viscous behaviour were observed for the other solutions examined.

The viscosity of a pseudoplastic liquid is dependent on the shear force to which it is exposed during atomization. The actual viscosity of the binder solutions is therefore unknown, a fact which possibly influences the correlation between viscosity and droplet size.

Influence of spray angle on droplet size

The spray angle is corrected by the setting of the air dome on the nozzle head. A decrease in spray angle results in a smaller droplet size (Table 4) due to the more intense contact between air and liquid, and this change in droplet size accounts for the previously described effect on granule size (23). Since only a slight influence on droplet size is observed at higher values of spray angle, the effects of air dome settings 5 and 1.2 on granule size could not be separated (23).

Influence of mass ratio and liquid flow rate on droplet size

Comparison of experiments at varying liquid flow rates is facilitated if atomization is described by the air-to-liquid mass ratio at the nozzle (Table 1).

By a two-factor analysis of variance the influence of both liquid flow rate and mass ratio were found (Table 5) to be significant at the 0.1 %-

Table 4. Influence of spray angle on droplet size (d_{50}, µm).
Binder solution: Gelatine 4 %, 40° C. Liquid flow rate: 150 g/min.
Air flow rate: 10 Nm^3/h.

Air dome setting		
2 (ca. 30°)[a]	5 (ca. 40°)	1.2 (ca. 60°)
56	89	100

[a] The values given in parentheses are spray angles.

Table 5. **Influence of liquid flow rate and air-to-liquid mass ratio on droplet size (d_{50}, µm).**
Binder solution: Gelatine 4 %, 40° C.

Mass ratio	Liquid flow rate (g/min)		
	100	150	200
1.15	129 123	99 113	98 98
1.43	106 102	90 86	79 88

level, whereas no interaction was observed. It is evident that a slight change in mass ratio results in an appreciable change in droplet size in accordance with the results of *Kim & Marshall* (13). For unchanged values of mass ratio an increase in liquid flow rate gives a higher air flow rate and thus an increase in the dynamic force of atomizing air (13). This accounts for the fall in droplet size observed at higher values of liquid flow rate.

Influence of liquid orifice on droplet size

The liquid orifice of the nozzle can be exchanged without affecting the area of the annular air orifice. Three different diameters are available, and to examine a possible interaction the experiments were carried out at two levels of mass ratio (Table 6).

By analysis of variance the effect of mass ratio was found to be significant at the 0.1 %-level in agreement with the above-mentioned results, and the effect of the liquid orifice was significant at the 5 %-level, while no interaction was found. The smallest liquid orifice resulted in the largest

Table 6. Influence of liquid orifice and air-to-liquid mass ratio on droplet size (d_{50}, µm).
Binder solution: Gelatine 4 %, 40° C. Liquid flow rate: 150 g/min.

Mass ratio	Diameter of liquid orifice (mm)		
	1.2	1.8	2.2
1.15	145 133	111 112	114 120
2.01	66 89	57 74	64 73

droplet size, whereas the effects of the orifices of diameters 1.8 and 2.2 mm could not be separated.

A slightly pulsating liquid flow due to the pump was observed when using the smallest orifice, indicating a lower limit of the diameter below which atomization is incomplete. Provided the liquid orifice is wide enough to permit a uniform flow, the diameter has no significant influence on droplet size.

Derivation of a droplet size equation

When comparing the results in Tables 4, 5 and 6 with droplet sizes calculated from reported equations (8,13,15) no agreement was found. Variation of the constants in the equations gave no satisfactory accommodation of the experimentally estimated droplet sizes. Differences in nozzle construction used may account for the inapplicability of the existing equations.

Consequently, experiments were carried out with the purpose of deriving an empirical droplet size equation to be used for describing the atomization in the present nozzle. Mass ratio, binder concentration and flow rate and temperature of the liquid were varied within the size range that is generally used for fluidized bed granulation, and the influence of viscosity and surface tension was examined. Due to small variations in the surface tension of the solutions employed no correlation was found between surface tension and droplet size. All experiments were carried out in duplicate, and the results are shown in Table 7.

The liquid temperature is expected to affect droplet size because of the influence of temperature on viscosity. Since this influence is greatest at higher viscosities, solutions of CMC and Kollidon 90 were used to examine the effect of liquid temperature. Analysis of variance lead to ambiguous conclusions, and the fact that the experimental error exceeds the effect of temperature might account for this.

Graphical presentation of the results on logarithmic paper indicates a linear correlation between droplet size and, respectively, mass ratio $\left(\frac{M_a}{M_l}\right)$, liquid flow rate (w), and viscosity (μ_l) corresponding to a correlation described by the power function $y = b \cdot x^a$. Examples are shown in Figs. 3, 4 and 5.

By analysis of regression it was concluded that with a few exceptions the correlations between droplet size and, respectively, mass ratio and liquid flow rate could be described by straight lines in logarithmic coordinates, whereas the correlation between viscosity and droplet size seems to depend on type of binder. It appears from Fig. 4 that CMC results in a

Table 7. Influence of binder solution on experimentally determined (Exp.) and calculated (Calc.) (Eq. (4)) values of droplet size (d_{50}, μm) under varying experimental conditions.

Liquid temperature[a]	Liquid flow rate	Mass ratio	Water[b]		Gelatine			Kollidon 90			CMC			Kollidon 25			MC		
			d_{50}		Conc.[c]	d_{50}		Conc.[c]	d_{50}		Conc.[c]	d_{50}		Conc.[c]	d_{50}		Conc.[c]	d_{50}	
°C	g/min		Exp.	Calc.	%	Exp.	Calc.	%	Exp.	Calc.	%	Exp.	Calc.	%	Exp.	Calc.	%	Exp.	Calc.
40	150	1.15			2 (1.5)	104 98	97	2 (5.6)	147 134	121	2 (5.7)	114 111	121	6 (1.6)	111 105	98	1 (3.0)	113 120	109
40	150	0.86	101 108	112	4 (2.6)	155 139	142	4 (18.6)	206 187	199	3 (10.7)	147 148	181	10 (2.6)	140 128	142	2 (8.2)	158 143	173
		1.15	94 96	84		111 112	106		159 133	148		125 135	135		114 109	106		132 116	129
		1.43	61 69	68		90 86	85		131 149	119		98 86	109		92 82	85		115 101	104
		2.01	43 41	48		57 74	61		108 119	85		48 46	77		51 44	61		52 75	74
		2.58	37 31	37		43 45	47		89 78	66		45 42	60		37 43	47		48 43	58
	100	0.86	105 114	133		167 199	168												
		1.15	115 97	100		129 123	126		168 151	176		144 143	160		163 132	126		131 135	153
		1.43	89 95	80		106 102	101												
		2.01	63 69	57		83 79	72												

		2.58	40 42	44		64 51	56												
	200	0.86	111 116	99		126 134	126												
		1.15	89 77	74		98 98	94		161 162	132		108 94	120		106 97	94		130 106	114
		1.43	54 46	60		79 88	76												
		2.01	39 32	43		71 67	54												
40	150	1.15			6 (4.3)	138 129	116	6 (50.4)	185 210	176	4 (20.4)	122 129	151	14 (4.3)	125 100	116	3 (19.5)	121 144	150
40	150	0.86			8 (7.1)	178 154	169	8 (117)	518 428	271	6 (69.4)	142 148	248	18 (7.1)	146 132	169	4 (48.3)	140 147	233
		1.15				134 150	126		326 268	203		117 122	186		103 122	126		132 136	175
		2.58				79 75	56		147 146	90		59 48	83		44 45	56		68 59	78
80	150	1.15						4 (6.7)	137 143	125	3 (4.1)	112 105	115						
80	150	1.15						8 (35.5)	223 228	166	6 (18.4)	126 124	148						

[a] The temperature of solutions of MC was 30° C.

[b] The viscosity of water was 0.65 cP.

[c] The values given in the parentheses are viscosities in cP.

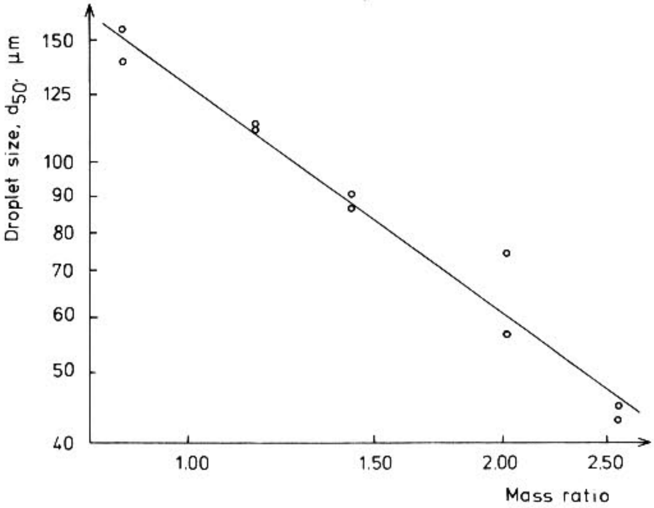

Figure 3. Correlation between air-to-liquid mass ratio and droplet size. Binder solution: Gelatine 4 %, 40° C. Liquid flow rate: 150 g/min.

smaller and Kollidon 90 in a larger droplet size than might be expected on basis of the regression line, with increasing deviations at higher viscosities. The results cannot be explained solely by the slightly pseudoplastic properties of CMC and Kollidon 90, in that mechanical properties of the binders, such as tensile strength (10) may influence the droplet size.

To obtain an approximate droplet size equation the correlation between viscosity and droplet size was described by the estimated regression lines.

The value of the exponent in the equation, $d_{50} = b \cdot x^a$ (where x is

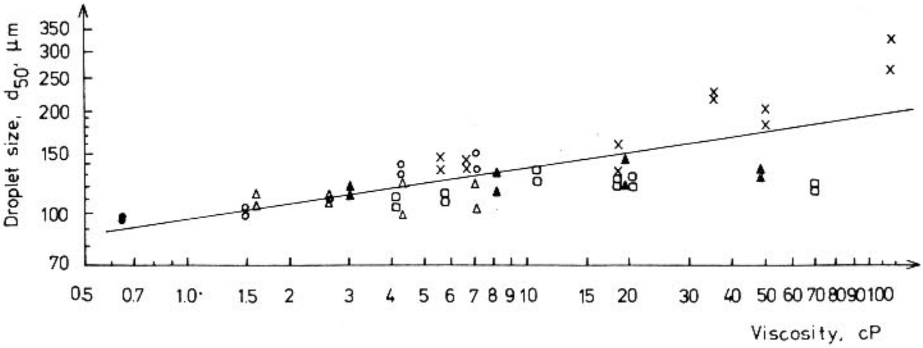

Figure 4. Correlation between viscosity and droplet size. Liquid flow rate: 150 g/min. Air-to-liquid mass ratio: 1.15.

●: water	△: Kollidon 25	○: gelatine
□: CMC	▲: MC	x: Kollidon 90

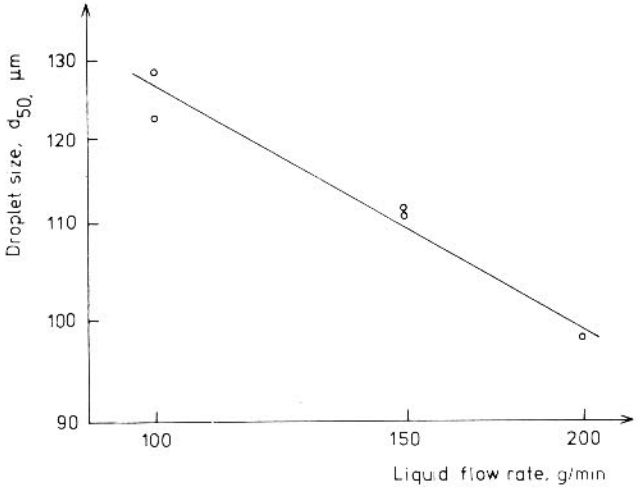

Figure 5. Correlation between liquid flow rate and droplet size.
Binder solution: Gelatine 4 %, 40° C. Air-to-liquid mass ratio: 1.15.

mass ratio, viscosity and liquid flow rate, respectively) was estimated as the mean value of those found to describe the correlation between droplet size and the variable in question at the varying experimental conditions. The following correlations were found:

$$d_{50} = b_1 \cdot \left(\frac{M_a}{M_l}\right)^{-1.00} \tag{1}$$

$$d_{50} = b_2 \cdot \mu_l^{\,0.17} \tag{2}$$

$$d_{50} = b_3 \cdot w^{-0.42} \tag{3}$$

where b_1, b_2 and b_3 are constants depending on the other experimental conditions. Eqs. (1)-(3) were combined into a single equation

$$d_{50} = 852 \cdot \frac{\mu_l^{\,0.17}}{\left(\frac{M_a}{M_l}\right)^{1.00} \cdot w^{0.42}} \tag{4}$$

where d_{50} is expressed in µm, viscosity in cP, and liquid flow rate in g/min. *Kim & Marshall* (13) found a similar influence of mass ratio, but a greater influence of viscosity.

Eq. (4) is valid when the present nozzle with an air dome setting in position 5 and a liquid orifice of 1.8 mm is used. The applicability may be questionable when using another nozzle construction, non-aqueous solutions, or experimental conditions, which deviate appreciably from the investigated values of mass ratio, viscosity and liquid flow rate.

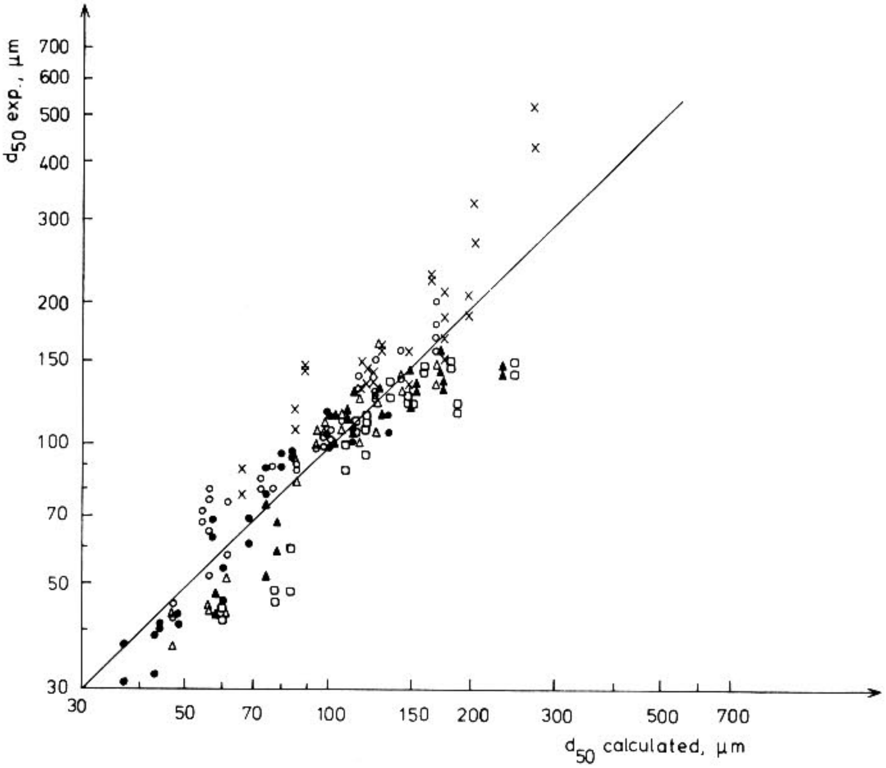

Figure 6. Correlation between calculated (Eq. (4)) and experimentally determined values of droplet size on basis of the results in Table 7.

●: water △: Kollidon 25 ○: gelatine
□: CMC ▲: MC x: Kollidon 90

The agreement between calculated and experimental values of droplet size is shown in Table 7 and Figure 6.
When viscosity exceeds ab. 50 cP, considerable deviation is observed due to systematic differences between the binders. At lower viscosities eq. (4) can be used for an approximate estimation of the droplet size of atomized binder solutions.

Droplet size distribution

Since droplet size distribution did not follow the usual distribution functions, such as normal, log-normal or square root normal, it was described by the mass median diameter, d_{50}, and x^*_{95}, x^*_{90}, x^*_{75}, x^*_{25}, x^*_{10} and x^*_{05}. The reduced diameter x^*_y is defined as d_y/d_{50}, where d_y is the droplet diameter, corresponding to the y-% of the cumulative weight distribution.

Table 8. Influence of mean droplet size (d_{50}, µm) on droplet size distribution characterized by the reduced diameters (x*) calculated on basis of results from experiments in Table 7. The values given in parentheses are relative standard deviations (%) of the reduced diameters.

d_{50}	x^*_{95}	x^*_{90}	x^*_{75}	x^*_{25}	x^*_{10}	x^*_{05}
< 70 µm	2.46 (16)	2.09 (14)	1.51 (10)	0.69 (10)	0.49 (15)	0.34 (26)
85-125 µm	1.91 (10)	1.67 (8)	1.34 (5)	0.66 (6)	0.40 (7)	0.31 (9)
> 140 µm	1.88 (11)	1.70 (11)	1.36 (7)	0.69 (6)	0.44 (11)	0.32 (12)

The results indicate that the reduced diameters depend on mean droplet size, and consequently mean values of x^*_y were calculated within three different size ranges of d_{50} (Table 8). Droplet size distributions differed only slightly when d_{50} exceeded ca. 85 µm, whereas smaller droplets showed a wider size distribution. However, it was apparently not affected by other factors such as binder and binder concentration.

The logistic equation described by *Pearl* (17) was previously used (13) to characterize droplet size distributions. The same method was applied to the results in Table 8, and the following equation, showing the relation between cumulative weight distribution (Φ_v) and reduced droplet diameter (x*), was derived:

$$\Phi_v = \frac{1.047}{1 + 21.3 \cdot \exp(-3.17 \cdot x^*)} - 0.047 \tag{5}$$

Due to differences in nozzle constructions used the values of the constants differed from those found by *Kim & Marshall* (13), as shown in Fig. 7 where the distribution functions are compared with experimental values. The results agree with eq. (5) when droplet size exceeds ca. 85 µm. A wider size distribution is observed at smaller values, but no accordance with the equation of *Kim & Marshall* is found. Since actual droplet sizes in fluidized bed granulation generally exceed 70 µm, eq. (5) is suitable for an approximate description of droplet size distribution.

Conclusions

Since variation of droplet size distribution seems to be impossible at maintained values of mean droplet size by use of the present nozzle, an atomized binder solution is ordinarliy characterized solely by the mean droplet size. It is shown that this is influenced by the type of binder, especially at higher viscosities. However, further experiments concerning the binder properties are necessary to explain this influence.

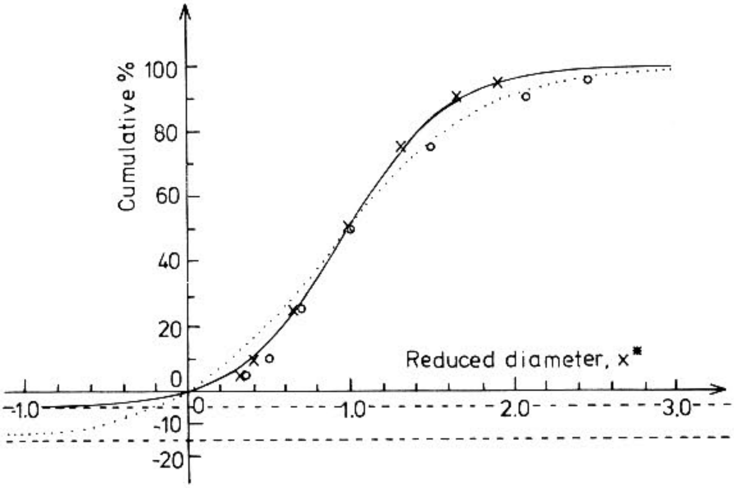

Figure 7. Comparison of droplet size distributions (by weight) described by *Kim & Marshall* (13) .... and by eq. (5) ———— with experimentally determined droplet size distributions (Table 8).

○: $d_{50} < 70$ μm x: 85 μm $< d_{50} <$ 125 μm

At viscosities below ca. 50 cP the empirical equation derived can be used for an approximate prediction of mean droplet size, which is primarily influenced by mass ratio, liquid flow rate, and viscosity of the solution. Varying the air flow rate is a simple and sensible way of altering the droplet size without changing the wetting and binding properties of the solution and consequently the most suitable way of controlling the granule size, provided that further experiments confirm the assumption of a correlation between droplet size and granule size.

Acknowledgement

This work has been supported by *Statens teknisk-videnskabelige Forskningsråd.*

References

1. *Bürkholz, A.:* Chem.-Ing.-Tech. *45,* 1973, 1.
2. *Davies, R. E. M. & J. M. Rowson:* J. Pharm. Pharmacol. *9,* 1957, 672.
3. *Davies, R. E. M. & J. M. Rowson:* J. Pharm. Pharmacol. *10,* 1958, 30.
4. *Davies, W. L. & W. T. Gloor:* J. Pharm. Sci. *60,* 1971, 1869.
5. *Davies, W. L. & W. T. Gloor:* J. Pharm. Sci. *61,* 1972, 618.
6. *Fraser, R. P. & P. Eisenklam:* Trans. Inst. Chem. Eng. *34,* 1956, 294.
7. *Golitzine, N.:* National Aeronautical Establishment, Canada. Note 6, 1951.
8. *Gretzinger, J. & W. R. Marshall:* AIChE J. *7,* 1961, 312.
9. *Gupte, A. R.:* Pharm. Ind. *35,* 1973, 17.

10. *Healey, J. N. C., M. H. Rubinstein & V. Walters:* J. Pharm. Pharmacol. *26* Suppl., 1974, 41 P.
11. *Jandl, G. & O. Bell:* Brennst. Waerme Kraft *26*, 1974, 313.
12. *Kassem, M. A. & A. G. Mattha:* Pharm. Acta Helv. *45*, 1970, 18.
13. *Kim, K. Y. & W. R. Marshall:* AIChE J. *17*, 1971, 575.
14. *Möbus, W.:* Cesk. Farm. *18*, 1969, 109.
15. *Nukiyama, S. & Y. Tanasawa:* Trans. Soc. Mech. Eng. Tokyo *4*, 1938, no. 14, 86, no. 15, 138. *5*, 1939, no. 18, 63. *6*, 1940, no. 22, 11, no. 23, 11 (ref. *Masters, K.:* Spray Drying. Leonard Hill, London 1972).
16. *Ormós, Z., K. Pataki & B. Csukás:* Hung. J. Ind. Chem. *1*, 1973, 475.
17. *Pearl, R.:* Medical Biometry and Statistics, 2. ed., W. B. Saunders Co., Philadelphia 1930, p. 417.
18. *Pigford, R. L. & C. Pyle:* Ind. Eng. Chem. *43*, 1951, 1649.
19. *Prioux, P., D. Lefort des Ylouses, M. Seiller & D. Duchene:* J. Pharm. Belg. *30*, 1975, 132.
20. *Reif, A. E. & C. Mitchell:* Ann. Allergy *17*, 1959, 157.
21. *Rouiller, M., R. Gurny & E. Doelker:* Acta Pharm. Technol. *21*, 1975, 129.
22. *Schmidt-Jørgensen, J.:* Dan. Tidsskr. Farm. *27*, 1953, 37.
23. *Schæfer, T. & O. Wørts:* Arch. Pharm. Chemi Sci. Ed. *5*, 1977, 51.
24. *Stawitz, J.:* Pharm. Ind. *14*, 1952, 59.
25. *Thurn, U.:* Mischen, Granulieren und Trocknen pharmazeutischen Grundstoffe in heterogenen Wirbelschichten. Diss., Zürich 1970.
26. *York, J. L. & H. E. Stubbs:* Trans. ASME *74*, 1952, 1157.